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EPITHELIOMA OF THE FACE

WITH SPECIAL REFERENCE TO THE TREATMENT

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INTRODUCTION.

Epithelioma of the face deals with that type of malignant tumor arising from the skin of the face which imitates the epithelium from which it arises, that is, the squamous epithelium. The cells have in a measure the same life history as squamous epithelium, though they are no longer growing on a flat surface, but are inclosed in spaces and become packed into masses. With a strange but distinctly and truly human perversity, the epitheliomatous eruptions of the skin of the face have in many instances been taken for warts, granulomas, herpes and syphilis. In a differential diagnosis of growths of the face, epithelioma should be one of the first conditions to be considered, and much caution should be exercised in making a final comitment even after a thorough study of the cases have been made.

When one considers that epithelial growths both benign and malignant are so common, that they are easily diagnosed, that the tissue from them is readily obtainable for histiologic study, and that most of them are so amenable to early treatment, it is surprising how much ignorance prevails concerning them even among the medical profession. Of all the forms of malignant disease, cancer of the skin is the easiest to recognize early because it can be seen and does not have to be deduced from various, possibly vague, symptoms. Yet many patients are seen who have been delayed so long in applying for treatment that a formidable procedure is required for cure, and in some cases palliation only can be attempted, the condition having progressed beyond any probability of complete removal.

In a recent survey it was estimated that five out of every

200,000 people in the United States died because of cancer of the skin, gathering from this roughly that the number suffering in one year would be ten times the number of deaths; the large figure is due to the long duration of the skin cases as a rule, and the rapid cure in many others. This in a measure gives an idea of the incidence of epithelioma of the face, for it has been found that 70% of all epitheliomas occur on the face, the remaining 30% being found elsewhere on the body. On the face, practically speaking, it has been found that the division of the 70% is as follows: lips 20%, nose 16%, and eyelids and associated structures 13%. The remainder are distributed over the forehead, cheeks and ears.

It has been found that males are more prone to the development of epitheliomas than are females, with a ratio of four to one. Blonds are especially liable and dark skins are relatively free, the condition being rarely found in negroes and Indians. From the time of the earliest medical writings to those of the present day, cancer has been defined and discussed as a disease of middle and late life; malignant disease is likely to be excluded from the realm of probability when the patient gives his age as twenty-five or less. Especially is this true of epitheliomas, that is, those forms of neoplasm that arise from the epithelial structure in contradistinction to those of connective tissue origin, the sarcomas. The youngest patient mentioned in the literature with squamous cell epithelioma was a boy fourteen, and the youngest patient having a basal cell growth was eleven.

The cause of skin cancer is about as much in the dark as that of all other kinds of cancer. It was formerly believed that lesions were so common on the face because of exposure of men working in wind, cold and the conditions connected with an

outdoor life. This seems to be exploded with the increase of city life and the evidence of just as much skin cancer among city office workers proportionately as among farmers and lumbermen. At one time it was popular to consider the irritation of unremoved dirt as a cause; certainly with the advent of modern plumbing and the use of more efficient soaps, the world must be cleaner than it was a generation ago, and yet the proportion of patients with skin cancer is the same. Also there seem to be just as many victims in the so-called upper strata, socially and financially, as in the lower, so that personal hygiene seems to play little if any part. Whiteman(68) believes that the greater the hybridization of a race, the more chance for cancer. To him the intermarriage of races introduces new factors of heredity and also an element of instability by which the tendency to carcinoma is increased.

Etiology and occupation are often intimately bound up in the causation of epithelioma. Injuries of various kinds such as the rubbing of a jagged tooth or dental plate, bruises, or anything that will cause a repeated injury and irritation to the tissues may be a factor. The tearing off of mucous membrane of the lip by smokers who allow the cigarette papers to stick, the heat and mechanical irritation of a pipe-stem, cuts and burns, are all exciting elements. Cancer develops in scars from old burns not infrequently, particularly if they have healed slowly and with considerable irregularity. This is a strong argument for the increasing use of skin grafting to speed up the healing of burns. One type of burn is particularly prone to be followed by cancer, and that is the repeated, slightly destructive effect of radium or x-ray over a period of years.

In addition to the above mentioned, there is a large group

of skin conditions which are perfectly safe and benign in themselves, but which if allowed to remain for years in some cases, take on malignant change and become cancerous. These were termed pre-cancerous by Hartzell(27), and the term has been commonly used since, although the term seems to be a misnomer and is open to great deal of criticism. Heimann(33) and Sutton(75) have been foremost in criticising this term and it seems that the term 'potential cancer' would express it more nearly. Etymologically speaking, the word precancerous implies that the condition must eventually terminate in cancer, however, this is not the case for the term is used with the understanding that through observation the conditions frequently lead to carcinoma. Heimann and Sutton maintain that on the theory that malignancy sets in when mitotic figures appear and control of the growth is lost, no matter what the size of the lesion, that it is impossible to determine when the true precancerous lesion becomes cancerous; therefore it would be impossible to use the term correctly, taking it from its exact meaning. They have found, mostly Sutton, that epitheliomas develop more frequently from normal skin than from the so-called precancerous lesions. From this it can plainly be seen that there are types of lesions which can only be termed as early cutaneous carcinoma and there are those that are potential carcinoma which have been more commonly termed precancerous.

Potential carcinomatous lesions(precancerosis) are important in the fact that they are potential ground for the development of cancer, and they should receive early and proper attention by removal of the lesion before the development of cancer. Heimann(33) has formed an outline which may aid some in classifying these types of growths:

Congenital

Malformations--Naevi, especially those that are pigmented.

Dystrophies-- Xeroderma pigmentosum.

Acquired

Inflammation

Hyperkeratoses

Seborrheic keratomas

Inveterate psoriasis

Leukoplakia

Horns

Specific Inflammations

Lupus Vulgaris

Lupus Erythematosus

General Inflammations

Ulcers and fistulas.

Physical Agents

Exposure-- Sailor's carcinoma

Actinic rays-- roentgen carcinoma

Chemical Agents

Arsenic, paraffin, soot.

Regressive Changes

Senile keratomas

Malformations

Dermoid cysts

Scars from any causes, especially syphilis, lupus, burns.

Epitheliomas may rise from any of the common dermatoses as senile keratoses, warts, seborrheic keratoses, leukoplakia, psoriasis, papillomas or cutaneous horns. It has long been known that prickle cell carcinoma may develop in the scar of burns, injuries, syphilis and tuberculosis; it has been known

to occur in a vaccination scar, the scar itself representing a past process. Any unhealed ulcer that remains an open sore for a considerable time may become the seat of a cancer, as occurs frequently in cracks of the lips. Substances that may lead to conditions favoring carcinomatous degeneration of the skin are tar, pitch, soot, paraffin, aniline dyes, arsenic and tobacco. Tobacco is without a doubt partly responsible for the epidermoid growths on the lower lip as is evidenced by the sex incidence.

Early workers in roentgen ray, especially in the medical fields, before protection was developed and understood, fell victim to radiant energy malignancies. The sequence has been burns, followed by dermatitis, keratosis, ulcer, carcinoma and metastasis. Repeated small doses daily acted on the damaged skin to bring about the ultimate result. King states(72) that Burrows has written several articles on the relation of cancers of the skin to focal lesions in other ectodermal structures. He claims that he has seen several skin carcinomas with breast metastasis which disappeared after removal of diseased teeth. He claims to have found lesions in the teeth in every case except one of breast cancer.

The sebaceous cyst has been found to be potentially carcinomatous. It is common in both sexes and is due to a shutting off of a hair follicle or sweat gland. Oil and perspiration continues to gather and a sac filled with cheesy material is formed. The process may continue for many years or may remain stationary; cancer develops from the wall of the cyst. This rarely occurs before sixty years of age. The growths on the face and scalp seem to be the most likely to undergo malignant changes.

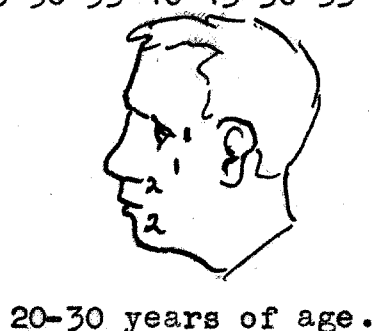
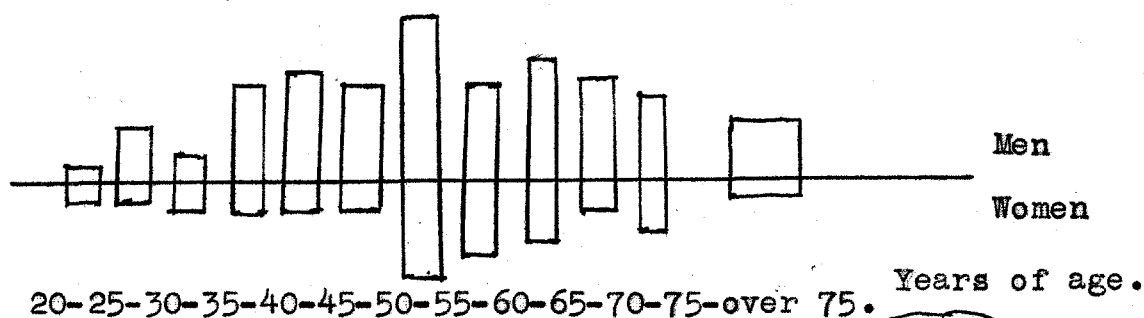
Warts may take on cancerous changes, and in older people

is often mistaken for what is cancer from the start. Keratoses are common conditions of the skin in later years and are found mostly on the exposed surfaces. There are two main types, keratoma senile and keratoma seborrhea, they are very similar and are difficult to distinguish even histiologically. The diagnosis is of great prognostic value, for the former is very prone to undergo malignant changes, while the latter very rarely does so. The senile keratosis also closely resembles senile verruca which are not potentially cancerous. These lesions appear as flat, raised, or verrucous areas which are sharply circumscribed, and are brownish to yellowish-brown in color, with keratosis and scaling. Block(3) believes that they may be dyskeratotic without being malignant, as do Bowen(7) and Darier(18); however, this is disputed by some.

Almost everyone has one mole or more on some part of the body, and these sometimes develop into cancer. These naevi are mostly benign, but seem more apt to become malignant when they are located at sites of repeated rubbing and irritation. The most common type is the soft white or light-brown pigmented mole. Both types do not commonly become cancerous, but to be safe they should be completely removed. It is, however, important to remember that when treated they should be completely removed, inefficient treatment may be of such an irritant nature as to set ^{up} a malignant change. Naevi with or without hair and whether light or dark colored, and however large, rarely become malignant. One type in particular needs special consideration and that is the birthmark which is mottled brown or blue, slightly raised, and verrucous in part of its extent. If there is the least change in size, elevation, or color, treatment should be instituted immediately. If it is thoroughly removed there is

very little chance of local recurrence and no chance for metastasis unless this has occurred previous to the excision.

Paljtschewsky(71) has charted and diagrammed the areas of epitheliomas on the face, their frequency, and the comparison between men and women. He believes that basal cell growths arise from a previous process in the sebaceous glands, hair roots, comedones, papules or nevi.



20-80 years of age, distribution in men and women is practically the same.

Frequently there are seen circumscribed epithelial newgrowths which are difficult to classify. Some of them develop into carcinoma. Sutton(75) has made a study of a series of cases in an attempt to determine whether this type of growth is malignant. He maintains that in many instances the early cutaneous lesions arise from normal skin, and discards the fact that they must arise from some type of precancerous condition as does Bloodgood and many others. Sutton in the same article describes the earliest recognizable skin carcinoma from three standpoints: the clinical, the microscopic, and the theoretical. Clinically, they are circumscribed epithelial lesions that have arisen de novo, and are generally brownish, rough, scaly or verrucous in character, asymmetrical, asymptomatic or slightly pruriginous, occurring by predilection on surfaces exposed to sunlight or irradiation, especially in persons with a sun-sensitive skin. Microscopically, they manifest epithelial irregularity, acanthosis and dyskeratosis, with changes in the cell type of the order of abnormal mitoses and atypical morphology, and with evidence of probable proliferative extension into a dermis that is characteristically infiltrated to a greater or less degree with round cells in the immediate region of the epithelial abnormality. Theoretically, they are interpreted as colonies of progeny of mutant epidermal cells, with retained capacity for proliferation, and lost responsiveness to growth control on the part of the host. Such a description is independent of the size of the lesion, in accordance with the theory that one cell can constitute a cancer. It is independent of the rate of growth of the lesion, for the progression may be so slow as to never to interfere with the well-being of the host. It stresses the concept that carcinoma

in the gross is purely a manifestation en masse of epithelium growing abnormally. It conceives relative malignancy as dependent on balance between proliferative capacity of the tumor cells and the resistance of the host. It explains multiplicity of cell type in one tumor on the basis of mutation following on mutation. Sutton believes that this enlarges the concept of skin carcinoma, and it offers a reasonable and unified conceptual design for the interpretation for neoplastic disease. It is eminently practical, for it encourages suspicion of minute lesions which might grow into gross carcinomas. If a lesion has a structure not compatible with a likelihood of its being early cancer, it might be called precancerous although the term is indecisive and undefinable.

Epithelioma of the face, according to Babcock(76), in its later stages presents a fairly characteristic picture. Advanced age of the patient is one of the salient points. The lesion usually appears as an ulcer, or a scabby, fungous or papillary growth, the ulcer has thick, swollen, indurated, everted edges, and a sloughing crater-like center. The more serious squamous cell epitheliomas begin at the mucocutaneous junctures and metastasize very early to the regional lymph glands. Basal celled growths occur chiefly in the middle third of the face, and spread to the mucous membrane from the cutaneous surface. There are four types: nodular, ulcerative, ciccratizing and cystic.

According to King(72) the growth, spread and life history of the three main types of epithelioma of the face are quite different. It depends on the pathology as to the type. The squamous cell carcinoma cells break through the basement membrane early and enter the lymph vessels by which they are carried to the regional lymph nodes. From these nodes the

cells may enter the blood stream and be deposited in any part of the body. The size of the primary lesion makes very little difference. Basal cell epithelioma almost always occurs above a line drawn from the angle of the mouth to the upper border of the pinna of the ear. However, it must not be forgotten that rapidly growing lesions in this region may be a squamous or transitional typed growth, which do metastasize to the cervical lymph nodes.

Broders(13) in numerous cases cited on his studies of carcinoma in situ has come to the conclusion that malignancy is not based on whether the cells have broken through the basement membrane, but agrees with Bloch(3) that it depends on the histologic picture. They believe that a lesion is malignant when it shows irregular epithelial proliferation, irregularities in structure, unrest in cells, atypical mitotic and amitotic figures, dyskeratoses and reactive inflammation of adjacent structures. Therefore it is essential to examine all suspicious lesions of the precancerous group for they may be an insidious early carcinomatous process.

King(72) has classified epithelioma of the face into three distinct types, and these are recognized by most authorities, namely, basal cell, squamous cell, and the baso-squamous or transitional cell growths. The basal cell epithelioma or rodent ulcer is a chronic, relatively slowly progressing ulcer which is usually anywhere on the face, nose, neck or ear and begins as a small flat papule or small warty growth, and remains in that condition for a long time. Eventually it breaks down into an ulcer which enlarges until it may eat off a large piece of the affected part. The ulcer as a rule is ~~is~~ shallow, but occasionally it eats deeply until it

reaches the bone or fascia where it is checked for an indefinite time. Finally it destroys these deeper structures. From the beginning on close observation a characteristic definite pearly, rolled border can be detected. This is very diagnostic; after the ulcer edge is thickened and indurated, the center secretes a liquid that crusts and becomes a black or brown scab. This usually has a clear base under it when removed, sometimes there is a drop of pus under the crust. The ulcer may be raised above the surrounding skin, may be soft and spongy, and reddish or brown in color.

The squamous cell epithelioma differs from the basal type in that it is far more malignant and metastasizes early into the lymph channels. King(72) states that one type of squamous cell epithelioma appears as a warty growth, slowly enlarges and later spreads and ulcerates. This type frequently starts on the mucous membrane or the site of a scar or verruca, and is likely to be papillomatous or fungating. If ulcerated, the edges are undermining and the depth and induration deepens. The other type described by King begins as a depression which early becomes fixed to the underlying tissues and ulcerates early into the lymphatics. Traub and Tolmach(65) have described the growth as the development of a nodule, usually rapidly, beginning frequently as a papular lesion of pin-head size, and reaching the diameter of one to two centimeters in from three to six weeks. After this period, the growth is somewhat slower. In patients under forty-five years of age the rate is more rapid than in older people. The typical squamous cell epithelioma of the glabrous skin begins first as a small grayish nodule covered with a scale or crust. As it increases in extent and depth, the crest assumes a reddish color and

may become ulcerated or verrucous. The tumor which develops is hard, firmly embedded in the skin, and yet protuberant. Its raised, bulging border presents a glazed waxy appearance. The presence of numerous small blood vessels in the border gives the base an acute inflammatory appearance which is characteristic because of the invasive tendency. The upper and outer portion of the border is usually more or less hyperkeratotic and in the central area the erosion appears. The latter develops into a perpendicular ulceration which is irregular, fissured, grayish in color and bleeds easily even upon slight irritation. On the floor of the central crater there are seen yellowish-gray granules, these are composed of horny cells and of epidermic globules.

Montgomery(45) says that basal cell epithelioma is not a morphologically closed entity, but may through metamorphosis become a baso-squamous(transitional) or even a squamous cell epithelioma at any time. Moreover, he found transitional epitheliomas presenting features of both basal and squamous cell growths in 12% of a series of cases. A positive diagnosis can be made only by microscopic examination and sectioning.

(72) (38) (21) (19) (36)

HISTORY

The ancients knew cancer well. They treated it by excision and by a variety of escharotics, including the Egyptian arsenical ointment. Cancer is mentioned in the Papyrus Ebers(B.C.-1500) and in the oldest remnants of the literature of India and Persia. Hippocrates(B.C.-460-375) received from earlier days a considerable body of descriptive facts regarding cancer of the skin and he first classified them as indolent ulcers and progressive malignant tumors. The humoral theory of pathology disseminated conceptions of the origin of cancer, for all disease was based on a deficiency or excess of the four vital fluids. Herodotus mentions that Hippocrates burnt out a carcinoma of the neck, the earliest record of diathermia.

Celsus was responsible for classifying growths into the following states: induration, cancer occultus and cancer apertus. Galen(A.D.- 131-203) failed to make any significant advance in the concept of cancer, but the presentation of the humoral doctrine in his writings formed a scripture which dominated the medical thought for a thousand years. To them, cancer developed from the concentration of black bile. Diagnosis rested chiefly on the cause of disease, while treatment of skin cancer by excision, ligation of vessels and cautery was comparatively successful. Leonides of Alexandria(A.D.-180) broke away from Hippocrates' conservatism and dissected out cancer extensively, cutting through healthy tissue with knife and cautery and approached closely to the modern technique of this operation.

In the Byzantine period(475-1500) considerable progress

was made in the description and classification of various tumors. In Arabia, Avicenna introduced the use of arsenic. Late in this period the ban of the church was extended from dissection of the corpse to the practice of surgery, but this could only be studied in private. Monks took to translating Galen's writings and began to speculate in alchemy, astrology and magic.

The Renaissance(1500-1700) bringing the invention of the printing press and also the discovery of the circulation of the blood by Harvey, greatly facilitated the spread of knowledge and aided more to accurate diagnosis and better treatment of cancer, but threw no light on the etiology. Andreas Vesal began the attack on many of the concepts of Galen, identifying deep seated cancer with ulcerating processes. Fabricius separated many inflammatory swellings from cancer, warned against incomplete removal in cancerous lesions, and experimented with internal remedies for a possibility of treatment. Paracelsus stands out as being the first successful opponent of Galen's theory of the humors in the late fifteenth century. At this time there was a distrust of Galen's authority and distrust of his crude theories on the etiology led to a complete demoralization in the treatment of cancer, encouraging great abuse of arsenic and other internal and external remedies. This permitted the faith cure career of Queen Elizabeth and developed many fantastic theories regarding the nature of cancer.

During the seventeenth and eighteenth centuries the common cause of cancer was based on the Lymph Theory, and Galen's doctrine was completely demolished and abandoned.

There was no appreciable change in the method of their treatment of cancerous growths. It was the general conception that the elements of cancer were fluid and traveled in the vessels. The Lymph Theory period was followed by the histiological period. With the construction of the achromatic microscope in Paris, 1824, a new era in cancer research was opened, a revolutionization in the theory of the pathological process taking place. Multiple theories were advanced for the cause of cancer which are direct precursors of the modern conception. Malignancies were classified and reclassified, with the resulting detailed classification of the present time. As for treatment, there still remained the principles that had been practiced through the earlier periods. G.A. Richter believed that possibly the malignancies arose from the blood, from scurvy, scrofula and syphilis, and that they should be attacked systematically. If, however, the cause could not be found, he only used those types of treatment which he had found to be beneficial on previous occasions, and he called these 'the empiricals'. He used these empirical methods to destroy the growth, and they included the following: quicksilver, arsenic, tartaric acid, hemlock and belladonna. Some of them were treated with venesection. The local treatment consisted of the withdrawal of blood together with that of forming draining sinuses in the neighborhood of the swelling; following this there was an excessive application of salves, poultices, vapours, and the sucking out of the swelling with leeches. Desault and Richter at this time treated the tumors by applying pressure to the growth and also by tearing it out. J. Hunter was the first to find that this often caused

recurrences and a firing up of the old lesion, and abandoned its use. DeHaen tried to heal with the use of the newly-discovered electricity. For rapid and radical removal they used the cautery with hot irons and corrosives; G.deSaliceto furthered the progress by ligation of circulation to the affected part followed by excision. With the advent of Heister, Bell and Camper, surgery was the elected form of treatment in malignancies, and all types of tumors for which there could be no cause determined, were immediately operated and the growth removed. Also, Heister found that one should not attempt surgery on any case that could not be completely removed. Petit and Bell removed all telangiectatic tumors with complete excision with the surgical knife.

In the nineteenth century electrical treatment became accepted, both the induced(Broca) and the constant(Langenbeck) current; electrolysis also was tried, however there were some who only restricted its use for use in thin-walled cysts and angiomas. The corrosives achieved an important part in treatment when introduced by Gendron and was later glorified by Girouard. These consisted in the application of zinc chloride pastes, potassium chloride paste was tried following this, and then many other preparations. The type of paste used in the application was determined by the particular demand. The application of heat took on a new form when Crusell tried galvano-cautery. This type of cautery was a predecessor to that of Paquelin who discovered the theory of thermocautery. During this time the application of cold was also frequently used in the treatment of tumors. Arnott in 1854 tried freezing the tumors for effect.

The process of ligation witnessed a period of popularity at one time following the successful results of Mayor in his treatment with ligation of the tumor en masse. Following this he constructed an artificial stalk from the non-pedunculated growths by a strong pull on the growth or by dissecting off the skin and muscle around the growth and thereby forming a stalk. Mayor's treatment lost popularity more and more during the last part of the nineteenth century, giving way to a partly similar type of treatment which consisted of squeezing out the growth following ligation which included cutting off the blood supply to the whole base; this method was introduced by Chassaignac in 1855. Later on, instrumentation was introduced by Charriere and Luer, they showed with it the danger of hemorrhage and the possibility of injuring the nervous elements. In more recent times Thiersch inaugurated the process of injecting substances which would cause a shrinking of the tumor. Such injections had been tried earlier but only on angiomatous tumors and those containing a liquid center. Thiersch used silver nitrate to destroy the growth, Senebier the gastric contents of dogs, Broadbent tried acetic acid, Billroth and Czerny used arsenic acetate; no satisfactory result was obtained in any of the methods tried. The process of enucleation introduced by Simon as a rule served only as a measure in palliative treatment.

The twentieth century opened as the experimental era, with the systematic study of tumors throughout the animal kingdom and a classification of tumors into distinct groups, which formerly were held only to be closely related. In the early part neoplastic diseases were only known in their

advanced stages and since poor results were obtained as a rule, interest in the study and experimentation was on a decline, with the result that treatment of cancer was left in the hands of quacks. Only within the last few years, as a result of scientific study, as a result of getting away from the unfounded theories and hypotheses of former generations, has there been uncovered the fact that something exists in cancer besides the terminal fatal, stinking, bleeding stage. Within recent years, doctors have followed through the events from the infliction of certain insults to and through the entire growth and course of the lesion. The picture has changed from one of abject, hopeless and black pessimism to one of reasonable optimism with a good incite into prophylaxis. Much has been learned about the so-called precancerous lesions and the advantage of removing them before they can become malignant. Recently there have been developed the relative values of various types of treatment as surgery, radium and cautery, and these will be discussed in detail in the section on treatment.

Reference on History -- (51), (47), (22), (34).

TREATMENT

The treatment of epithelioma of the skin of the face is first and foremost the proper treatment of the various afore mentioned potential cancerous lesions, the precanceroses. Prophylaxis is of the greatest importance and much can be done to prevent development of the neoplasm by attention to the precancerous dermatoses. The aim of the physician is not to treat the fully developed cancerous lesions as was true only a decade ago, but that of treating the contributory causes. This consists mainly in the removal of sources of repeated and chronic irritation and of any of the contributing exciting causes. It necessitates removal of tissue beds and the seats of inflammatory change which are suitable for development of the newgrowths. Advice should be given against exposure of the face to irritating substances, especially in those with sensitive skins; these include the effect of wind and sunburn, arsenic, or any of the prolonged irritating substances. Care should be taken in preventing overexposure to radiation in the handling of radium and x-ray which have become so popular in the new and modern methods of therapy. Irritation from smoking should also be borne in mind. (38) (72)

Since the precancerous lesions have been found to be so intimately related to the development of malignancy, they bear more than casual mention here. To be truly theoretical, the proper treatment would be to excise the lesions completely when they appear; but to recommend removal of every scar, every nevus, every keratoma when

everyone has at least one of these, or to frighten the public with tales of menace, is not justified by facts. The aim in prophylaxis is to prevent the formation of these precancerous conditions if possible. Williams(70) states further that the lesions should be watched when they appear and be protected from any sources of irritation, and if they are exposed to injury or when they show signs of change of character, they should be removed.

Darier(18) in his article on precancerous conditions of the face states that he believes the incidence of superficial cancer of the face could be greatly reduced by the early diagnosis of precancerous lesions. Of these, he regards senile keratosis and naevus as being between them responsible for at least 60% of cutaneous cancers of the face. Other of the potentially malignant growths are xeroderma pigmentosum, radiodermatitis, arsenical keratosis, scars of old burns, ulcers, fistulas, and lupus. The naevi which tend to undergo malignant change are mostly of the soft, warty cellular type. These may give rise to naevo-cancer at any age, even in the newborn. The change is heralded by an increase in the size of the growth and the appearance of a congestive border or of extensive pigmentation, with a sensation of burning or itching. The only effective treatment according to Darier is electrolysis or electrocoagulation.

Darier(18) believes that the senile keratoses should be treated by cauterization, galvanocautery or solid carbon dioxide; if, however, the keratotic patch is surrounded by a zone showing congestion with pruritis or a burning sensation, it should be destroyed at once by x-ray or radium. The

carcinoma arising from this type of keratosis is of the basal cell type. Sutton(62) in 1915 reported on cases of seborrheic keratoses and found them to be the forerunners of the ~~prickle~~⁵ cell variety of epithelioma. Sutton divided these keratoses into three different types according to their degree of development: early keratoid, advanced keratoid, and malignant. Together with Montgomery and Stellwagen he agrees that lesions that are potentially cancerous should be removed to prevent possible conversion into neoplasm. Treatment of the early keratoid lesions, according to Sutton, should be that of frequent application of bland grease to the lesion, such as rosewater ointment, with the occasional employment of lubricant later to prevent recurrence. One should never use hard water, highly alkaline soaps, or shave closely. In the advanced keratoid lesions, or the nevoid or verrucous types, the treatment is a little more drastic. It consists of the following measures: application of the salve of salicylic acid, sulphur and petrolatum; after this has softened the skin, it should be wiped off with benzine on cotton; it should then be frozen with carbon dioxide snow and an antiseptic applied. If the lesion is malignant, Sutton believes it should be immediately excised if the site is the forehead or lips, and should be x-rayed if it is nasal or orbital.

Excision is a favored way of removing these precancerous lesions for by this the entire process is completely removed, and there is no further potentiality of the growth to become malignant. When possible the precanceroses should be treated immediately, and the laity should be educated as to the

importance and potentiality of these lesions. In dermatitis caused by x-ray, Holfelder(35) has found that the use of the electrocoagulating current for the removal of the involved area is most successful. Sutton(63) believes that to prevent development of keratoses about the ears, the ears should be protected from frostbite, injury, etc. To combat keratoses there he uses a mild keratolytic following which he uses ^acarbon dioxide snow applied locally to the lesion. Grier(26) in a report of 71 cases of precancerous lesions, shows that by x-ray he completely cured 67 of these cases, the other 4 cases did not respond to exposure to the roentgen rays.

In considering lesions after they have become malignant, the element of time plays a large part in the treatment. After a lesion has become an epithelioma, the prognosis is much less favorable and becomes progressively worse as the course of the growth continues. Therefore it is urgent that immediate treatment be instituted. There are many and various methods of therapy, all of which, in the hands of reliable men, may give satisfactory results. The types of treatment, wherever the lesion may be located, are several in number. The most successful at present are radiation and surgery, although there are numerous reported regimes that seem to give as favorable results. Of radiation, radium and roentgen ray are the important standard methods, yet the galvanocautery, endotherm knife, electrocoagulation and the actual cautery may be used in certain cases as methods of surgery entailing the destruction and removal of the lesion. In treating any epithelioma, the problem is essentially not the agent one uses, but the use of an agent

which will completely destroy the growth.

In classifying epitheliomas pathologically for treatment, there are two main types to be considered, the basal celled and the squamous celled types. The transitional celled type may be classified for treatment from the points derived from the study of the other two, since it is made up of cells found in both. In reviewing the types of treatment it must be borne in mind the type of lesion that is being dealt with, especially its depth, extent, mobility and anatomical location; also one must consider the duration of the lesion, histology, probable radiosensitivity, and the effect of previous treatment.

Basal cell epithelioma is the more benign of the two pathological types and does not metastasize. Under adequate treatment the cures reach 90%. Finnerud(24) in explaining the failure to metastasize, states that the basal cells involve freely the lymph spaces of the corium, but are incapable of traversing the lymph channels and invading the lymph nodes. He, however, reports 2 cases in which there was secondary metastasis to the basal cell type, proving that metastasis is possible in these lesions, and is not entirely limited to the prickle cell variety. Since no other cases had been reported at the time, he considered them as possible anomalies and as an exception to the rule. The lesion is much more extensive subdermally than is anticipated and care must be taken in treatment to reach and include the whole process. Hazen(32) reports that most of the late cases of epithelioma of the face come after they have been treated by pastes, plasters, and even by

x-ray. He believes that x-ray heals the top of the growth while the deeper part of the lesion continues to grow in many of the cases; therefore he advocates roentgen ray only in inoperable cases and prefers surgery with removal of the entire process, either with the knife and the application of cautery to the edges, or actual excision with the cautery knife. McKee(44) received best results in the treatment of basal cell epitheliomas with surgery and x-ray. If surgery is used, the excision ~~must~~ be complete and a biopsy should be made of the excised part; if the margins contain malignant cells, there should follow x-ray to the part. He states that x-ray is good treatment in capable hands, and is especially good for those lesions in the canthus of the eye, lids, and alae where it is hard to apply any surgical procedure. Radium is good in places which cannot be reached with the x-ray, and has about the same effect; also the reverse is true in choosing x-ray. McKee believes that it is permissible to use curettage in small lesions following this with x-ray, this process seems to reduce the amount of x-ray needed. In deep seated growths of rodent ulcer he advocates the use of the knife, curette, caustics, dessication, and cautery, followed by intensive roentgen ray or radium. He has found that caustics and curettage leave a worse cosmetic result than other forms of treatment. F. Smith(56) in a report of cases advocates the regimen of treatment proposed by Sherwell which consists of the following: preliminary thorough curettage followed by cauterization of the base with silver nitrate. Then supplement this with intensive application of x-ray or radium. There is a good cosmetic result in this

type of treatment and is therefore very useful about the ears and eyes.

Squamous cell epithelioma is the more malignant of the types of growth being considered. The chief feature of this type is the possibility and probability of metastasis. The prognosis becomes more grave when this type of epithelioma is found to be present. Broders(12)(10) in 1920 reported on 500 cases of squamous cell epithelioma of the face and found that 59% of his cases were living at the end of three years, of which 93% reported a good result for an average of eight years. Of the 41% that are dead, one-half died of epithelioma. He found that results were not as good in those who used tobacco, because of the high percentage of inoperable cases that presented themselves in this group. He found that those who had been treated previously with plasters and pastes did not show very favorable prognosis. After metastasis had occurred the mortality jumped up to 82%, and no patient was reported living who showed involvement of the cervical glands, or who showed involvement of more than one set of glands. Broders(11) in 1919 reported best results in the treatment of squamous cell growths from one excision with the knife alone, or one excision with the knife followed immediately by cautery. Again he reports that results were not as favorable after the lesion had been previously treated with acid, carbon dioxide or any of the caustics. Hazen(32) thinks the ideal treatment is a block operation with a removal of the surrounding fat, fascia and muscle, with the lymph vessels and glands; if the glands are removed, the metastasizing cells cannot go any farther. The object is to remove the

entire growth, examine it histiologically and if it shows to be prickle cell in type, the regional lymph nodes should be excised. Montgomery(46) has found that squamous cell growths are usually relatively resistant to roentgen ray and radium treatment as compared with the basal cell type. Radiotherapy should be used as a last resort in the treatment of these cases. He believes that surgical treatment, with an unusually wide excision because of the insidious infiltration of the tumor cells, is indicated whenever possible. Epitheliomas are prone to recur, so a five year interval should elapse before a cure is pronounced. Prognosis should be guarded when the growth is of a transitional cell type, for this corresponds to the more malignant type of the squamous cell growth. Smith(56) in a treatment of cases which consisted of well-developed varieties and of some that had been previously treated, found that radium has only occasional value in the squamous cell lesions. Coagulation in association with mass removal afforded him the best results. Without gland involvement, he obtained the better results with electrocautery destruction of the lesion followed by radium. The value of prophylactic radiation or surgical dissection of uninvolved glands as a preventative measure is debatable. He treats recurring prickle cell growths by platinum radium needle implants, or with bipolar electrocoagulation.

Lundsford and Taussig(43) in analyzing their cases, found that in squamous cell epitheliomas without metastasis they obtained 50% cures clinically. They found that after metastasis had occurred the prognosis was poor and that

those treated received a small percentage of cures. In some of these cases, treatment made them worse. They concluded from their studies that squamous cell types were more resistant to therapy than the basal cell types, with a larger percentage of cures in the latter type. Patients having received previous treatment responded less rapidly to subsequent treatment, and the older the lesion, the more difficult it was to effect a cure no matter what the pathology. The cases reported by Lundsford and Taussig were treated with radium therapy, often in conjunction with x-ray, curettage, cautery, dessication or surgery.

The face is composed of several well-defined anatomical structures; so in further considering the treatment of epithelioma, the different methods used may be grouped according to their efficacy in the various areas on the face. The structures found on the face are variously shaped and are made up of several different types of tissue; they are, therefore, the source of considerable controversy in ideas on treatment, and are subject to many and diverse types of treatment. In arranging the sites of the malignant lesions to be discussed, they will be considered in the order of their frequency of occurrence in the various locations. The lips are the most frequently involved area, and next come the nose, eyelids, ears, cheek and forehead in order of frequency.

Cancer of the lips includes both the upper and the lower lip. Roughly speaking, the very benign basal cell epithelioma is the growth typical of the upper lip, and the squamous cell is that of the lower lip. Therefore the prognosis and the urgency of treatment is entirely opposed

in epitheliomas in these two areas. Cancer of the lower lip is about twelve times as frequent as that of the upper, about 95% of the cases occurring in males. Visceral metastasis is rarely present. Metastasis when it occurs from the upper lip growth, is first to the nodes adjacent to the submaxillary salivary gland, or to the upper deep cervical group. From the lower lip, the drainage is to the submental nodes and to the nodes surrounding the submaxillary salivary gland. This course of extension brought forth the importance of removal of the salivary gland in cases of metastasis, for the reason that numerous lymph nodes are in close relation to it and often occupy deep recesses in the gland substance although lying without its capsule. Brewer(9) has adopted Broders classification of epitheliomas of the lip and considers it a great contribution in perfecting operative technique. This classification grades the tumors into four classes ranging between those which show the greatest degree of differentiation with no mitotic figures to speak of, that cures show 100% (Type I); gradated to the type IV which shows the opposite microscopic picture with a percentage of cures at zero.

Smith(56) in choosing what he believes to be the best treatment for epitheliomas of the Lips, states that the prime purpose in the management is the elimination of the lesion, with proper consideration to the restoration of function and appearance. He believes that radium has only occasional value in squamous cell lesions and that coagulation in association with mass removal of the involved area produces the best result. Simmons(77) in his comment on Brewer's paper believes that the prime

purpose in treatment is extirpation of the lesion stating that operation is the treatment of choice in practically all cases of carcinoma of the lip, and does not employ radium. He believes that surgical removal is much quicker and causes the patient much less discomfort than radium. He further advises removal of the glands from one or both sides of the neck, depending on the location of the tumor in every case. Lain(40) agrees that radical removal of all the pathological cells is the primary aim of successful treatment. He reports a large percentage of cures with complete extirpation of the growth by surgery followed by a careful dissection of the metastasizing glands. To him, radium and x-ray, used either singly or together, is as satisfactory in a certain class of selected cases in the hands of experts and proficient radiotherapists. In considering the complete function of the lymph glands, it is reasonable to suggest that a certain degree of stimulation instead of extirpation is the more scientific method of preventing metastasis in certain classes of cases. Trueblood(66) uses radical excision with the radiocautery while the involvement is limited to the skin alone; if it has penetrated deeper, other methods of which irradiation is the best, should be used. Figi(23) is a staunch advocate of surgical treatment, removing the entire growth with later plastic reconstruction operations. If the growth involves less than one-third of the lip, and if it does not involve the bone, he completely excises the lesion with a V-shaped incision and closes the wound with primary intention. If the growth involves more

than one-third of the lip, and if it does not involve the bone, he removes the entire growth by surgical excision with following plastic operation at the angle of the mouth, which is best done by incising the angle and rolling up the mucous membrane. To equalize the lips, a wedge is removed from the cheek. If the growth has involved the bone, Figi believes in removal with diathermy or cautery, thoroughly cauterizing the area of attachment. The wound should be left open for a period of nine months for appearance of metastasis, and if it does not occur, a plastic reconstruction of the lip can be done.

Among those who favor radiation treatment in epithelioma of the lip, Quigley is foremost, treating them entirely with the use of radium. His method(51) of treatment varies according to the stage of the disease. In the earlier stages before the particles of the cancer growth have penetrated deeply into the lymph vessels, and before they have broken off and been floating in the lymph stream into the neighboring glands of the neck, the laying of radium tubes on the surface of the diseased lip directly over the diseased area is effective, using a combination of beta and gamma rays. The idea is to bathe the whole diseased area and the tissues beyond with a mixture of gamma and hard beta rays. If one gland is involved, it may be possible to implant radium needles in the gland and so destroy the disease at this point. As a rule, in cases with multiple gland involvement treatment is not attempted, but these cases are pronounced incurable. Brewer(9) has obtained very satisfactory results in the treatment of epitheliomas of the

lower lip with radium and x-ray primarily. Oschner(78) disagrees, and feels the treatment in early cases is radical operation with cautery, and believes that this should be insisted upon. He agrees that in late cases in which complete removal seems impossible, radiation may be used, suggesting that radium needles be implanted in a position beyond the margins of the growth, and x-ray should be applied properly to the neck. Then when the patient has recovered from the effects of this treatment, the lingual artery should be ligated, and the entire growth together with one centimeter of apparently healthy tissue surrounding it should be removed with the cautery. This should be followed with a careful excision of the lymph glands with the electric cautery, the incision of the skin being made with the knife. Pusey(49) believes in x-ray of the growth if there is glandular involvement, if there is no evidence of metastasis, he treated the condition by local and complete excision. In both types combined, he reports a cure of 28 out of 38 cases he treated. Abbe(1) reports that the pathological cells wandering in the lymph channels are more sensitive to an active agent such as radium or x-ray than are the cells in the circumscribed growth, and feels that these agents may be of some assistance in the treatment of the late metastasizing cases. Brewer(9) in summarizing the results of Dr. Quick states that the earlier reports on the treatment of cancer with radium and other varieties of radiant energy failed to impress surgeons as to its value in the early operative cases,

but that the results compare favorably with those reported in the surgical treatment; this is the result of the progress made in the technique of radiation procedures and in accurately estimating the proper dosage.

Brewer(9) in uniting the statistics of those clinics in which the five-year standard of cure has been adopted, and in which the highest type of technical work is being carried out, has obtained the following averages: group I, in which only the primary lesion was removed, showed that 66% were well and without evidence of recurrence after five or more years. Group II, in which the primary lesion and the anatomically related submaxillary lymph structures have been removed, but without lymph node involvement, reported a 92% five-year cure. Group III, in which the primary lesion and the related lymph nodes have been removed, but with the positive evidence of involvement of the latter, 34% five-year cures were obtained.

Next to the lips, the nose is the most frequent site of epithelioma on the face. Sutton(61) states that basal cell types make up the majority of the lesions here, while Quigley(51) says that the squamous cell is the predominant type. The prognosis depends on the type, location and the degree of involvement; in the prickle cell variety the outlook is serious, even with prompt and radical excision tissue destruction occurs. Sutton has described a relatively benign type of lesion on the nose which is called the Krompecher type. It requires conservative treatment and is the type of growth that is the harvest for the quacks with their paste and plaster treatments.

This type of growth is easily eradicated unless cartilage or periosteum are involved, or if the contiguous tissues have been destroyed by maltreatment. In the squamous cell type, the plan of treatment advised by Sutton is excision of the growth with the knife cautery followed by exposure to radium or x-ray. He believes it is wise to pursue a radical course and then follow up with repair work. In cases presenting involvement of cartilage, excision is preferable to radiotherapy. Sutton has outlined a line of treatment for cases of basal cell epitheliomas on the nose. It consists of curettage which is immediately followed by application of silver nitrate to cauterize the wound. This is then neutralized by the administering of soda after three minutes. This procedure should be followed by radium therapy. McKee and Hazen (79) feel that x-ray is satisfactory because of the comparatively superficial location of most of the growths here, using repeated short exposures for better cosmetic results. F. Smith(55) believes that surgery should not be used in lesions of the nose. King(72) feels that radiation is the method of choice in these epitheliomas. X-ray can be used where it is easily administered; small apertures like the nostrils are readily treated with radium and with difficulty by roentgen ray. A cross-fire effect on growths on the nose can be obtained by the use of radium in the nostril and the roentgen ray externally. In very deep cases of ulceration, with sloughing and involvement of the underlying cartilage and bone, any form of radiotherapy may fail to have any effect, in these

instances, surgery remains the method of choice. Quigley(51) has obtained satisfactory results with the application of radium. He states that in lesions involving the thick skin of the nose around the tip, the most common error is in using too small a dose of radium radiation. The growth here is progressing in skin of more than average thickness and roots extend more deeply than may be supposed, and a greater dose is required for the best effects; also, the dose may be increased here without much danger of injuring the structures underneath. In lesions on the bridge of the nose the dose must be decreased, however, this is usually of sufficient strength, for the growths located here tend to remain superficial.

Epitheliomas occur on the eyelids almost as frequently as on the nose. The eyelids may be the seat of a basal cell or of the squamous cell variety of epithelioma, and here there is often seen a squamous cell growth developing on a basal cell growth. Chernosky(16) has found that the basal cell type of growth, when not involving cartilage or bone, may be entirely removed by radium; it is more easily removed than the squamous cell type, and does not spread as rapidly. When a rapidly spreading growth is met with and previous radiation has failed, it should be removed by excision with the knife or cautery, and the open wound treated with radium. If bone is involved, complete removal of the lesion is indicated, thoroughly cauterizing the wound with the actual cautery or soldering irons, and applying radium to the open wound. A maximum dose always should be given at the first treatment,

as temporizing with small doses may only stimulate and thus aggravate the lesion, and the chance of eradicating the trouble is lessened. Rubber and lead screening are used by Chernosky to protect the eyes. The patients must be seen periodically for recurrence of the lesion, in which case treatment must be again applied before the condition has a chance to become more extensive. Laborde(39) reported absence of recurrence in 50 out of 56 cases with the treatment of radium. The order of occurrence of the types of lesions he encountered were basal 48%, transitional 29% and squamous 20%. He used radium needle implantations for better location of the radiation, and reported very little deformity from this type of treatment. Dusseldorp and Calderon(20) used electrocoagulation of the lesion, with surgical removal if there was any orbital invasion when radium failed to help; good results were reported. King(72) thinks radium is very efficient in the treatment of epithelioma of the eyelids; he prefers this to x-ray because it can be applied more accurately, this assuring an equality of radiation especially in the locations of the inner canthus where x-ray treats the high areas rather than the growth proper. McKee(44) thinks that x-ray is preferable for the lesions of the canthus of the eye and also the lids, not using surgery because it is hard to apply here. To protect the eyes he applies bismuth paste and gauze. In an attempt to combat cancer by increasing the resistance of the body, Murphy(80) has x-rayed the whole body. By this he attempted to cause a lymphocytosis, but none occurred and the radiation had no

effect on the cancerous growth. Quigley(51) states that early epitheliomas of the lids are easily cured by the application of radium. If the diseased process invades the orbit, the progress then becomes exceedingly rapid with invasion into the deeper parts of the orbit and metastasis to the skull soon occurs.

Epitheliomas of the ear are of particular significance because in this part of the face, anatomically, the skin is in very close proximity to cartilage. Cartilage shows a small degree of healing power because of the very small blood supply, and this makes the treatment in this area very difficult. Cartilage is quite resistant to radium, and this makes surgery the treatment of choice. Quigley(51) believes that radium should be applied to kill the growth, in sufficient dosage, with subsequent plastic treatment by surgery. Lehmann(41) believes that if the soft radiation fails to show response in the growth, it should be treated by radiation with gamma rays. Sutton(63) states that in cases presenting cartilaginous involvement radium and x-ray are useless. Radiation is good before involvement of the cartilage, but the radiation must be intensive. The healing process is retarded by irradiation, but repair may be aided by the application of silver nitrate cautiously. He has found that the growths are mostly of the basal cell type, and the majority develop from seborrheic keratoses which in turn develop from slow healing wounds. Sutton varies his treatment with the character, stage and extent of the lesion. Generally, prickle cell epitheliomas call for early

and radical excision, the basal cell types may be treated more conservatively with an attempt to obtain a better cosmetic result. He believes that actual cautery is good, but that the burns produced frequently cause the patient some discomfort; chemical caustics and arsenic pastes are permissible. If the lesion is extensive, the entire ear may be removed with healing over of the denuded area, with the aid of skin grafts if necessary. Hazen(30) has reported cures in cartilage involvement with the cautery.

Brewer(9) states that cancer of the cheek is rare and is an exceedingly malignant disease which quickly spreads to the upper and lower jaws and to adjacent structures of the mouth, with early involvement of the cervical lymphatics. In all but the earliest cases radical surgical treatment involves an extensive, disfiguring and dangerous operative procedure, with but little hope of permanent cure. For Brewer, treatment with radium application gave only mediocre results. Abbe(1) obtained 60% cures with the use of radium and heat. His method is excision and the application of cautery to the edges of the wound, or applying cautery directly by means of a hot soldering iron, with the subsequent application of radium. This is used when there is no metastasis. He believes that the administration of heat is of definite value in the treatment for it definitely arrests the growth, and the effect carries along the lymphatics for some distance. Lundsford and Taussig(43) have reported clinical cures in 67% of their cases, meaning a freedom of

symptoms for a period of at least one year. They found further that those coming after previous ineffective treatment, showed one-half as many cures. Brewer(9) suggests treatment in advanced cancer of the cheek by surrounding the growth with a row of radium needles one-half centimeter from the outer edge of the growth, and later excising with the cautery. He reports a three year cure of 35% in a small number of cases which were considered advanced when treatment was instituted.

Epitheliomas of the forehead are quite rare and require no special discussion in regard to treatment. The basal cell variety of growth is the most predominant pathological type found here and the treatment corresponds to that discussed under the pathological types.

Epithelioma of the face has been discussed from the standpoint of pathology and location, and now will be taken up from that of the various methods of treatment that have been employed and the efficacy of each. King(72) states that there is probably no better method than x-ray in selected cases, but if the lesion does not respond to a dose that is safe and sane, it is much better to resort to some other method or combination of methods. The results are equally as favorable with either roentgen ray or radium, for there is very little difference in their action. The selection of one over the other is merely a matter of convenience as far as the location of the area treated is concerned. Radium at times can be applied more accurately thus assuring an equality

of radiation; also the patient is spared the noise of the machine and the dimly lighted depressing atmosphere of the average roentgen ray room. When the radium is in place there is no necessity for the patient to remain in a fixed position and the patient may spend the time pleasantly. Occasionally a growth is found which is refractory to x-ray and which yields readily to radium. On the other hand, x-ray can be used to cover a more extensive area in a much shorter time. A combination of the two is very helpful in applying cross-fire, especially in very severe lesions.

Grier(26) has reported the following results with x-ray: from a study of 200 cases, a cure of 169 was reported, 16 recurred, and there^{were} 15 cases that failed to respond to the treatment. Chaoul(14) states that very favorable results have been obtained in Germany with x-ray where radium is scarce and x-ray treatment is very highly developed. The good results are gotten from the administration of a high voltage method, and also from the fractionated dosage method of Coutard. Williams(69) states that tumors of the lips are usually resistant to x-ray. He has been interested in the results shown in elderly individuals. He believes that x-ray is particularly beneficial in people too old to withstand an operation, or even anesthesia. Of the cases he has studied, he has found that the majority of them have had a cure for at least two and one-half years, and feels that the freedom from recurrence until the patient dies from an intercurrent disease is worth while in old individuals that only have a

few years to live. In a study of the end results of roentgen ray treatment, Hazen(29) has reported a cure in 84% of his unselected cases, and 93% cure in selected cases. He found that the results were better in women than in men and that the earlier the lesion, the better the result. Lesions previously treated with either radium or x-ray gave him only a 50% cure; of the recurrences, 94% of them appeared in the first year. In the prickle cell type of epithelioma he shows a cure of 45%, with gland involvement a 41% cure. He states that the roentgen rays affect the growth by stimulating the tissue about it to combat the cancer cells, and also acts by retarding the mitosis. Radium acts by giving a caustic result on the lesion; and deep, heavy cross-fire acts by causing an atrophy of the vessels.

The value of radium in the treatment of face epitheliomas measures up to that of x-ray, and in some cases may be superior because of the convenience it affords. In reviewing the statistics of the Radium Hemmet in Stockholm, Magnusson(52) reported results on 783 cases. He reported a three year cure in 77.3%. Of these cases, 63 cases showed recurrence in three years, one-half of these occurring in the first year. The prognosis was based on the size of the lesion and the mode of growth, and not on the histiological picture. He states that the prognosis was much less favorable when the lesion reached the area of four centimeters. Smith(56) describes the Curie and Regaud methods of applying radium, these being used more or less as a standard in radium treatment.

In superficial lesions, treatment consists in the application of screened surface contact with the growth, using the full strength, flat, glazed applicators. In deep seated and extensive growths, molds seem to be preferable. The molds or blocks of tubes are set at a distance one centimeter from the skin, the dose is sixty millicurie hours per square centimeter. The dose may be given singly or in multiple doses. Smith states that this method of treatment is especially effective about the eyes and lips. He believes that x-ray is of value in post-operative treatment, and when used as such, cuts down the percentage of recurrences. When it is used it should entail hyperintensive, massive doses, going as high as two to three times the erythema dose. Benson(2) has suggested the use of unfiltered radon in small doses for treatment, the tubes being either upon the skin or interstitially placed. Hazen(29) says that the younger the person having the growth is, the better are his chances for cure, this^{is} contrary to the consensus of opinion on the relationship between age and the degree of malignancy, and is open to dispute. Sequiera(53) has reported a cure after five years in an individual nineteen years of age. The lesion was treated with radium, and was of the basal cell type. The youngest aged individual in which epithelioma has occurred, is eleven. Bradley and Snoke(8) reported a case in 1927 with extensive involvement of the side of the nose and cheek which was shown to be of the prickle cell type on biopsy; the treatment consisted of the application of unfiltered radium for one hour.

The result was a complete cure, with no evidence of recurrence after a three year interval. This case brings out the value of radium in advanced cases, and should be seriously considered in the treatment in the cases of inoperable tumor. Traub and Tolmach(65) feel that radium or x-ray are of use only as adjuncts to surgery, both before and after removal, and do not advise it because of the refractoriness of tumor cells to radiation. King(72) states that the objections to radium therapy to be considered are acute radium dermatitis of a severe grade, subsequent wrinkling and telangiectasia. However, in expert hands there is very little danger of this, or of its sequelae. The action of radium is just about an inch around the area of implantation, therefore in treatment this should be borne in mind and enough needles placed to cover the entire growth. Emanation from radon seeds is good, for the effect is for about three weeks and the emanation is constant, acting by their effect on the constantly appearing young and immature cells of the growth. Radium must act in short intense doses to prevent destruction of tissue.

Chernosky(16) is an advocate of radium in the treatment of epitheliomas. He says that in early superficial lesions radium gives good results, with minimum scarring. The application of radium encourages the sufferer to apply early for treatment, since the therapy when properly used, and in sufficient amount, is harmless and painless. Unless the lesion is very extensive the patient may pursue his daily duties while receiving

the treatment. Chernosky believes that if the radium treatment is unsuccessful, surgical measures may be resorted to without detriment to the patient. He believes that by combining radium therapy and surgery, the percentage of operable cases can be increased and, by the use of radium radiation as an after treatment, the number of recurrences can be markedly reduced.

Many use radium and x-ray radiation as an adjunct to some other method such as excision or coagulation, the latter being used to remove the primary growth. Stevens(59) has outlined a treatment which institutes the use of coagulation of the lesion with subsequent use of radiation. His first step is the complete destruction of the lesion with the electrothermic coagulation current, using the Ouidin current for small growths and the d' Arsonval for the large ones. He begins the process in the healthy tissue beyond the edge of the diseased area thereby sealing off the lymph and blood drainage, and then follows with curetting or scissoring out the burned tissue. In basal cell growths he follows the coagulation with irradiation of the area immediately; in the squamous cell type, in addition to the local radiation, it is applied over the draining lymphatics. The treatment should be completed as nearly as possible in one sitting. He finds also that previous treatment with caustics, radiation, etc, effect a more difficult cure. He has reported very good results with radium, showing a 100% cure in superficial cases, from one to five years, and 90% cure in the deep cases. He, however, has not classified the growths

pathologically and it is possible that a majority of them were of the benign basal type of growth. King(72) has used a similar type of therapy and has reported very favorable results. After coagulating the growth, he gives from two to three and one-half units of unfiltered x-ray, screening from one-fourth to one-half centimeter from the border with lead. Next, he screens to the border of the lesion and gives one unit of unfiltered x-ray. This is to be repeated in from four to six weeks. In the superficial growths, no filter is used; in the deeper ones, filtration is necessary to get the proper penetrated rays into the tissues, and to cut out the longer, more caustic rays which cause burns.

The combined use of radium and surgery in the treatment of epithelioma of the face has been quite extensively used in recent years. Strauss(58) in the treatment of epitheliomas after metastasis to the neighboring lymph nodes has taken place, has brought forth the combined use of radium and surgery. When metastasis has occurred, he believes that x-ray or radium must be applied to the glands of the neck whether they are palpable or not. If they are palpable, he waits from six to eight weeks after the last radiation treatment and then does a block dissection of all the glands of the neck on the one side, or on both sides if the lesion is situated close to the midline. If excision is delayed until the glands break down, it will be too late for this type of treatment. Strauss is convinced that x-ray alone will not destroy carcinoma cells in the cervical lymph nodes.

The above described treatment of Strauss pertains particularly to epitheliomas of the lip.

Surgeons as a rule are the men that favor surgical treatment for epithelial tumors of the face, although all are willing to concede that radiation is a necessary adjunct. It would be almost impossible for any surgeon, no matter how capable, to solve the optimum dose of radiation for the many and varied types of tumors that are treated; however, with the assistance of the radiologist, the combined judgement of the two should materially decrease the percentage of failures in treatment. Excision is advised for the small early cases when the process of treatment will not mutilate the face, and will thereby free the face of the entire growth; this^{is} especially advised in basal cell epitheliomas unless they are deformed or if they are very extensive. Traub and Tolmach(65) in reviewing the various types of treatment for face malignancies, have favored surgical treatment. They state that in treating some of the older patients showing lesions of long duration and slow growth, radiation is sometimes advisable, but that even in such instances unless there is some other contraindication to this procedure, radical excision should be given the preference. In reviewing the various types of excision, they state that removal by knife is effective, but the objection to this method is that there is excessive bleeding and there is the frequent necessity, especially in large wounds, of resorting to skin grafting in order to obtain a good cosmetic result. This method has been criticized on the

grounds of possible dissemination of the cancer cells through the blood stream, but recent opinions have held this possibility a doubtful one. Actual cautery knife destruction of the growth by a criss-cross grid leaving the charred area in situ as a crust, is effective, but eliminates the benefit of a microscopic report on the excised tissue. One cannot always be certain when employing this method that the center of the base is entirely destroyed unless it is overcauterized. Traub and Tolmach(65) state that the favored method is excision with the electric knife or endotherm. The incision is made so as to complete a deep trench about the tumor, leaving a sufficient margin. The walled-off area is then cut out, stopping the bleeding with the coagulation current. One must make sure that the base of the growth is carefully excised. If the base of the wound has not been irradiated after removal, the wound usually heals in about four to six weeks; radiation delays the healing about one to two weeks. If the wound is large, and upon healing there is left a hypertrophic area of tissue in the central portion, this may be reduced with radium, or may be excised. Even in wide removal of large growths these men have reported satisfactory cosmetic results in the use of the electric knife.

Acid or chemical applications of any kind used cautiously and in small amounts, serves only to aggravate a lesion. (65) Effective destruction by acid usually entails severe, extensive and unsightly burns, and this method should be discouraged as acceptable treatment.

Caustic pastes and plasters are included in this group.

There have been many modifications of the basic type of treatment in epitheliomas previously discussed. Some are highly theoretical, all in an effort to find some means of controlling one of the most dreaded of afflictions, cancer. Sherwell(57) believes in thorough, deep and efficient curettage of the lesion followed with immediate application of an escharotic (60% mercuric nitrate), with perhaps several applications. This then is neutralized with an alkaline medium of sodium bicarbonate, and then salt is pressed into the wound. He allows the scab to remain in place until repair from underneath pushes it off. Bordier(5) uses diathermy preferably because with it he has found that the wound heals more rapidly and recurrence is less apt to occur. Tarabuchin(64) has advised the use of potassium sulphocyanide applications for the treatment of cases because it is very inexpensive and very cheap to use. He reported a cure of 24 out of 25 cases for periods of a year or less, however, these statistics are unsatisfactory for comparison with previously mentioned types of treatment and their results. Cheattle(15) has done extensive study on the comparison of the incidence of carcinomas, leucodermas and sclerodermas on the face, and also of the location of these growths. He finds that areas of epitheliomas on the face are the same as those of leucoderma and scleraderma, all of them occur where the cutaneous end branches of the nerves pierce the skin, that is, where the nerves become cutaneous. He has denervated these areas and the growths have ceased

spreading. He also has found that infections do not occur as frequently in these areas. From the evidence he has gathered, he has taken up the belief that the cause of cancer is neurotrophic; he concedes that it is apparent from this that the cause of cancer is more trophic than microorganic. Oxon(73) has reported quite favorable results with the intracutaneous injection of oil of cinnamon or sodium cinnamate into the growth. This surrounds the area and supposedly causes a leucocytosis by stimulating the lymphocytes to transform into the more adult form of leucocytes. In the same way, it also causes an organization of cells of the tumor by effecting them to become less genetic in type and to become regulated. Oxon also has used the oil injection treatment previous to surgical removal as an adjunct. Purely hypothetical, Luden(74) has shown that the cholesterol content of the blood promotes cell multiplication, in both normal and malignant conditions. He proved further that radium reduces the cholesterol content of the blood in his experiments on animals. Theoretically, radium decreases the cholesterol content which in turn causes a decrease in cell multiplication, and should in this way inhibit mitosis and decrease the degree of malignancy present. This has not usually been taken into account as one of the beneficent effects of radium in the treatment of malignancies.

In addition to the curative treatment of malignant growths, Quick(50) has classified the therapy as palliative and psychological. In his article he continues:

the general medical care of cancer is too often overlooked, or, for the moment, forgotten under the stress of the immediate problem. Malignant disease may and does exist in conjunction with many other grave medical conditions. This is particularly true since the so-called cancer age is also the period in life during which the system begins to show the effects of wear and tear in general. No strenuous therapeutic procedure, operative or otherwise, for cancer should be undertaken without careful unbiased approval of the patient's general condition quite apart from the immediate problems incident to the malignant condition itself. Secondary involvement by metastasis should always be suspected if other symptoms arise. General medical supportive treatment should ever be kept in mind and carried on vigorously in conjunction with the specific treatment of the tumor bearing area. Anemia is almost always associated with malignant disease except in the early stages. It may be increased by irradiation, especially if it is very heavy. If irradiation be prolonged, or repeated at intervals, the character of the anemia changes. Liver and iron therapy have been a God-send to cancer therapy.

It may also be of great value to encourage the cancer patient, and one should not hesitate doing this whether the benefit be mental or physical. Reference to the word 'cancer' is in itself enough shock to break the morale of any patient, even in the most stoical type of individual. It is detrimental to use the term without restriction and also to be too frank in one's statements

to the patient. The patient who is able to maintain his balance and with whom everything can be discussed frankly and fully at all times, is rare. The manner, rather than the amount that is told the patient, is of the greatest importance. It is possible to give the patient an incite into his case without shattering his morale by severing the last thread of hope to which he clings. By the exertion of a little tact, after appraising the situation, one may give a very honest impression to the patient without disturbing him mentally to the degree that a simple blunt statement of facts might do. Unless the morale can be maintained, the therapeutic measures are bound to fail.

Palliative treatment is instituted in the relief of pain and the control of symptoms, even while recognizing the inevitable termination of the case. Prolongation of life is unjustifiable unless it is attended by a reasonable degree of relief from symptoms; foremost among these symptoms are pain and the unpleasantness of irritating discharges and foul odors. Fortunately, with the advent of radium, this situation has been remedied, and the patient may be spared some of the horrible conditions in terminal cancer. Transfusion is made use of best in the preparation of the patient for operative procedures. As a rule sedatives should be used for restlessness in the patient, and anodynes for the relief of pain. In using an anodyne, care should be taken to avoid the addictable drugs as long as possible; the use of physical agents and sedatives should be encouraged

rather than the use of any drugs. Morphin should only be used as a last resort and in the terminal stages, when the length of treatment will be short and there is no great possibility of developing a tolerance or an addiction to the drug. The same holds true for the local application of cocain, for a great deal of this drug is absorbed, even from the involved area itself. Codeine in considerable amounts is preferable to beginning the use of morphin. In the selection of measures to relieve pain and discomfort, the simplest are always the best. Drugs which depress the patient's morale are to be avoided as much as possible.

COMMENT

Epithelioma of the face is quite common, constituting about 30% of all cancers. The face serves as the site for the majority of cutaneous epitheliomas, 70% of them being found here.

The cause of epithelioma is still obscure, as is the cause of cancer, but there are many so-called exciting factors that can be eliminated to reduce, in a measure, the occurrence of these growths.

There are lesions which in themselves are benign, but seem to be predisposing sites for the subsequent development of malignancy. These precancerous lesions, as they are commonly termed, are potential areas of malignancy and bear watching. They are sometimes confused with an insidious early carcinoma.

The treatment of precancerous lesions is removal. This may be done surgically, by cautery and coagulation, dessication, keratolytics or by the irradiation methods. At any rate they should be completely eradicated to prevent any possibility of following neoplasm. It is permissible to treat these conditions conservatively, removing all possibilities of irritation and watching for any changes in the size of the growth, in which case radical removal is imperative.

The best results obtained in the treatment of

epitheliomas are in the early cutaneous lesions in which treatment is instituted for the first time. The public should be educated and the physician trained to recognize these early growths, and effective therapy should follow immediately. In these early cases, radiation and any of the surgical procedures are equally effective in obtaining satisfactory results.

Treatment of the epitheliomas of the face have been discussed in three catagories, pathologically, as to location, and as to the various proposed types of treatment and the relative value of each. The pathological types show two varied modes of growth, prognosis, and urgency in the establishment of therapy. The basal cell type is slow growing, generally non-metastasizing and quite benign, having an excellent prognosis if gotten early, and treatment in it is not exactly urgent. However, care should be taken to completely remove the growth, for recurrence is quite common. In contra-distinction, the squamous cell epithelioma is a rapidly growing and an early metastasizing growth, and carries a guarded prognosis. Treatment should be instituted immediately and there should be careful examination for evidence of metastasis.

As to location, the treatment seems to be a matter of preference. The presence of pathological types seems to be the important gauge as to the kind of treatment required. Attention should be given

to the possibility of metastasis and also of involvement of cartilage or bone, in which case adequate therapy must be given.

In considering the various types of treatment that are employed, it seems that surgical excision and either x-ray or radium are the methods of choice. In surgical excision, the coagulation knife seems to be the instrument of choice, being of value both in aiding hemostasis and in sealing off the lymph and blood vessels to prevent further spread of the growth. X-ray and radium show as satisfactory results as does excision, the choice of one or the other being governed by the ability of either to satisfactorily penetrate the treated lesion in its entirety. Radiation is of particular value in treating lesions that are too extensive for surgical excision, the so-called inoperable tumor. It also has achieved success in palliative measures by relieving the patient after all possibility of cure has vanished. Many modifications of the basic principles in treatment have been introduced recently, together with various original creations, in an attempt to control cancer. They all carry their satisfactory percentage of cures, and probably are effective in veteran hands.

CONCLUSION

I have concluded that the basis of good treatment is early recognition of the malignant condition with prompt adequate treatment. There is no need for improvement of methods if this is carried out. Although radium and x-ray work equally as well, I think surgical excision is the preferable procedure in early lesions of epitheliomas providing satisfactory function and cosmetic results can be obtained. Excision could easily be followed by radiation to the involved area, especially in suspicious cases. After metastasis, removal of the involved set of nodes with subsequent radiation to the lymphatics is advisable. In inoperable cases and in cases needing palliation, radium and x-ray are of unequalled value. Psychology and general medical care in late cases of epithelioma are as essential as the specific local therapy.

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